

**Koisio technology-produced water significantly decreases the blood flow velocity
of both carotid artery and radial artery of human subjects**

Youjun Zhang^{1,*,#}, Mingchao Zhang^{2,*}, Weihai Ying^{3,#}

¹Department of Cardiology, Huadong Hospital Affiliated to Fudan University,
Shanghai, P.R. China; ²Multiscale Research Institute of Complex Systems, Fudan
University, 220 Handan Road, Shanghai, P.R. China; ³Med-X Research Institute and
School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai 200030,
P.R. China

*: These authors contributed equally to this work.

#: Corresponding authors:

Youjun Zhang

Department of Cardiology

Huadong Hospital Affiliated to Fudan University

Shanghai, P.R. China

Weihai Ying, Professor

School of Biomedical Engineering and Med-X Research Institute

Shanghai Jiao Tong University

Shanghai 200030, P.R. China

E-mail: weihaiy@sjtu.edu.cn

Abstract

High blood flow velocity occurs in patients with such cardiovascular diseases as hypertension and arteriosclerosis, which can lead to complications of these diseases. Therefore, it is of medical significance to invent novel approaches to slow down the high blood flow velocity. Oxidative stress can lead to pathological alterations of blood vessels, such as vasoconstriction, which can produce accelerated blood flow. Since our previous cell culture study has shown that Koisio technology-produced water (KW) has antioxidant capacity, in this study we tested our hypothesis that KW may be able to slow down the high blood flow velocity of human subjects. Our study has shown that KW intake significantly decreased the blood flow velocity of both right and left common carotid artery of human subjects. KW intake also significantly decreased the blood flow velocity of both right and left radial artery. Collectively, our study has indicated that KW has the capacity to slow down the blood flow velocity of both common carotid artery and the radial artery. It is warranted to conduct future studies to determine the effects of KW on the cardiovascular system and to investigate the mechanisms underlying the effects.

Keywords: Blood flow velocity; Carotid artery; Radial artery; Koisio water; Oxidative stress

Introduction

Prolonged high blood flow velocity can lead to sustained elevated shear stress, which is an important contributor to vascular narrowing and atherosclerosis¹. High blood flow velocity occurs mainly in patients with hypertension and arteriosclerosis, which can cause the complications of these diseases². Hypertension can lead to accelerated blood flow velocity, which is further heightened in patients with arterial stenosis or excessive vascular tension^{3,4}. Therefore, excessively high blood flow velocity is a risk for cerebrovascular diseases. It is of medical significance to discover novel approaches that can decrease high blood flow velocity to normal ranges.

Oxidative stress plays significant pathological roles in multiple cardiovascular diseases such as hypertension and myocardial ischemia⁵⁻⁷. Oxidative stress can lead to pathological alterations of blood vessels such as vasoconstriction, which can produce accelerated blood flow velocity⁵. Since our previous cell culture study has shown that Koiso technology-produced water (KW) has antioxidant capacity⁸, in this study we tested our hypothesis that KW may be able to slow down the high blood flow velocity of human subjects. Our current study has indicated that KW has the capacity to slow down the blood flow velocity of both common carotid artery and the radial artery of human subjects.

Methods

Measurements of the blood flow velocity of human subjects

This study was conducted according to the ethics protocol approved by Huadong Hospital affiliated to Fudan University (Approval #: 2024K286). Upon arrival at the ultrasound examination room of Huadong Hospital affiliated to Fudan University, all volunteers rested for 30 minutes. After the rest period, baseline measurements were taken, and a Doppler ultrasound system (GE LOGIQ E8 high-resolution color Doppler ultrasound system) was used to assess the blood flow velocity in the left and right radial arteries (LRA, RRA) and left and right common carotid arteries (LCCA, RCCA) before KW drinking. Immediately after the measurements, the subjects drank 700 ml KW. One hour after the first measurements, the second measurements were conducted.

The ultrasound probe was positioned axially to locate the distal portion of the artery, with markers placed on the skin. The probe was then aligned perpendicularly to capture circular images of the arteries. During Doppler spectrum measurements, efforts were made to display an extended segment of the vascular lumen to align the artery's long axis with the ultrasound beam or reduce the angle between them. The Doppler angle was adjusted to 60 degrees to measure peak systolic velocity (PSV) and end-diastolic velocity (EDV). To minimize errors of the measurement which are caused by arterial deformation from probe pressure, the pressure was carefully reduced to clearly visualize the arterial lumen. All ultrasound data were photographed for archiving and recorded accordingly.

Statistical Analysis

Data were presented as mean \pm SEM and analyzed by one way analysis of variance (ANOVA) followed by Student-Newman-Keuls *post hoc* test except where noted. *P* values less than 0.05 were considered statistically significant.

Results

We measured blood flow velocity of both the left and right common carotid arteries of the human subjects before and after KW intake. In the left common carotid artery, KW drinking led to a decrease in the blood flow velocity: The blood flow velocity was 84.87 ± 3.05 cm/s before the KW intake, while the blood flow velocity was 77.29 ± 2.57 cm/s after the KW intake (Fig. 1). In the right common carotid artery, KW drinking also led to a decrease in the blood flow velocity: The blood flow velocity was 83.73 ± 2.52 cm/s before the KW intake, while the blood flow velocity was 69.02 ± 2.63 cm/s after the KW intake (Fig. 1). All of the changes of the blood flow velocity were statistically significant.

In this study there were multiple people who had particularly high blood flow velocity (> 100 cm/s) in their either left or right common carotid artery mainly before the KW drinking. We conducted analyses on this group of subjects: There were 94% of the subjects who had the blood flow velocity higher than 100 cm/s either in their left or right common carotid artery before the KW intake (Fig. 2). In contrast, there were only 19% of the subjects who had the blood flow velocity higher than 100 cm/s either in their left or right common carotid artery after the KW intake (Fig. 2).

We also measured blood flow velocity in the left and right radial artery before

and after the KW intake. In the left radial artery, the KW drinking led to a decrease in the blood flow velocity: The blood flow velocity was 61.30 ± 2.65 cm/s before the KW intake, while the blood flow velocity was 53.52 ± 2.03 cm/s after the KW intake (Fig. 3). In the right radial artery, KW drinking also led to a decrease in the blood flow velocity: The blood flow velocity was 61.32 ± 2.59 cm/s before the KW intake, while the blood flow velocity was 54.06 ± 1.81 cm/s after the water intake (Fig. 3). All of the changes of the blood flow velocity were statistically significant.

Discussion

The major observations of this study include: 1) KW significantly decreased the blood flow velocity of the common carotid artery of human subjects; and 2) KW significantly decreased the blood flow velocity of the radial artery of human subjects. These observations have indicated that KW can decrease the blood flow velocity of both common carotid artery and radial artery.

The usual normal velocity of the common carotid artery is 30 - 40 cm/sec⁹. Although the velocity scale setting should be adjusted for each patient, elevated carotid artery blood flow velocity is primarily observed in cases of hypertension and arterial stenosis, which poses a risk due to the complications associated with these conditions¹⁰. Hypertension alone can accelerate blood flow velocity, and the presence of arterial stenosis or increased vascular tension can further increase blood flow velocity, signaling a heightened risk of cerebrovascular disease².

In this study, the data from the subjects whose blood flow velocity in the left or

right common carotid artery exceeded 100 cm/s before or after KW intake were analyzed. Results showed that before the KW intake, 94% of the subjects had blood flow velocity above 100 cm/s in their left or right common carotid artery. However, after KW intake, only 19% of the subjects had blood flow velocities above 100 cm/s. Additionally, the mean blood flow velocity decreased from 108 cm/s to 96 cm/s. This data suggests that KW can quickly (within one hour after intake) reduce the excessively high blood flow velocity of the common carotid artery in the majority of the subjects.

Water is a major component of life, occupying approximately 70% of the volume of the human body. The quality of drinking water can produce a significant impact on human health. Due to the significance of drinking water, it is critical to invent novel strategies to modulate the properties of water in order to discover novel biological functions of water. It has been reported recently that through certain physical modulations, a type of pure water that contains numerous ultra-small nanobubbles has significant antioxidant effects, in which the ultra-small nanobubbles play key roles in the antioxidant effects¹¹. Our previous study has shown that Koisio technology-produced cell culture media significantly decreased oxidative stress in a cell culture model⁸. Since oxidative stress is an important factor in pathological vasoconstriction, the KW-produced antioxidant effect may lead to attenuation of pathological vasoconstriction.

In our current study, we have shown that KW intake was capable of decreasing the blood flow velocity of both common carotid artery and radial artery, which provided support to our hypothesis that KW may slow down the high blood flow velocity. It is

warranted to further determine the effects of KW on cardiovascular systems, and to investigate the mechanisms underlying the effects.

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Figure Legends:

Figure 1. Drinking of KW led to significant decreases in the blood flow velocity of common carotid artery of human subjects. In the left common carotid artery (LCCA), the blood flow velocity was 84.87 ± 3.05 cm/s before the KW intake, while the blood flow velocity was 77.29 ± 2.57 cm/s after the KW intake. In the right common carotid artery (RCCA), KW intake also led to a decrease in the blood flow velocity: The blood flow velocity was 83.73 ± 2.52 cm/s before the KW intake, while the blood flow velocity was 69.02 ± 2.63 cm/s after the KW intake. #, $P < 0.05$; ###, $P < 0.001$.

Figure 2. Drinking of KW led to a marked decrease in the percentage of the subjects with excessively high blood flow velocity of the common carotid artery of human subjects. There were 94% subjects who had the blood flow velocity higher than 100 cm/s either in their left or right common carotid artery before the KW intake. In contrast, there were only 19% subjects who had the blood flow velocity higher than 100 cm/s either in their left or right common carotid artery 1 hour after the KW intake.

Figure 3. Drinking of KW led to significant decreases in the blood flow velocity of the radial artery of human subjects. In the left radial artery (LRA), KW drinking led to a decrease in the blood flow velocity: The blood flow velocity was 61.30 ± 2.65 cm/s before the KW intake, while the blood flow velocity was 53.52 ± 2.03 cm/s after the KW intake. In the right radial artery (RRA), KW drinking also led to a decrease in the blood flow velocity: The blood flow velocity was 61.32 ± 2.59 cm/s before the KW

intake, while the blood flow velocity was 54.06 ± 1.81 cm/s after the KW intake. ##, P
< 0.01.